REMARKS

This is in response to the Office Action mailed on August 23, 2004, and the document cited therewith.

Claim 7 is amended, claims 1 and 12-21 are canceled, and claims 22 and 23 are added; as a result, claims 2-11, 22, and 23 are now pending in this application.

Support for claims 22 and 23 is found throughout the specification, for example at page 4, line 35 to page 5, line 5 and page 8, line 31 to page 9, line 14.

Claim 7 has been amended to remove the phrase *and a derivative thereof.*

Applicants submit that these changes have added no new matter to the application.

Personal Interview

Applicants wish to thank Examiner Ewoldt and his Supervisory Patent Examiner Chan for extending the courtesy of a personal interview to Applicants' representative, Richard A. Schwartz, on December 7, 2004.

Applicants' representative noted that suitable cells for the method of the present invention are not limited to antigen-presenting cells, and may include cancer cells, for example. In addition, the term *stimulating an immune response* includes all aspects and types of immune responses and mechanisms for stimulating them.

Further, Applicants' representative pointed out that in Example 3 of Applicants' specification, transport of HRP from the cytosol, and not surface presentation, is being measured. The Examiner acknowledged that the method of Example 2 of Applicants' specification is enabled.

The Examiner continued to object to the phrases *and a derivative thereof* and *a lysomotropic weak base thereof* in claim 7. Applicants' representative presented the Examiner with a copy of a recent CAFC decision, *Bilstad v. Wakalopulos*, Appeal 03-1528, decided October 7, 2004, that requires the PTO to consider the knowledge of the artisan and the predictability of the art when making a written description requirement rejection. The Examiner requested one or more publications showing that lysomotropic weak bases were known in the art.

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out any deficiencies in his next communication so that Applicants can amend or supplement the interview summary.

§112 Rejection of the Claims

1. Enablement

Claims 2-11 were rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner stated:

(1) "the specification provides insufficient evidence that the claimed method could be used for expressing a molecule on a cell, said method comprising photochemical internalization wherein the molecule is sufficient to generate an immune response...." Office Action at page 2.

(2) "only certain antigen presenting cells are capable of presenting antigens and generating an immune response." Office Action at page 3.

(3) "costimulation [of helper cells] ... is required for the generation of an immune response." Office Action at pages 3-4.

(4) "[t]he disclosure of two related species of [photochemical internalization] agents cannot be considered to be reasonably sufficient to enable the method of the instant claims...." (Office Action at page 4) and "a few closely related agents is not representative, nor enabling of, the broad classes of agents set forth in the specification and claims." (Office Action at page 5.)

(5) "the specification does not sufficiently demonstrate the required limitation that the claimed method be capable of inducing sufficient MHC class I presentation of an antigen to generate an immune response.... Indeed ... Example 3, clearly demonstrates the opposite, the triangles of Figure 4 show a lack of antigen on the surface of the cells." *Ibid.*

This rejection is respectfully traversed.

With regard to the allegation that insufficient evidence has been presented illustrating that the methods of the invention can be used to express antigens on a cell, Applicants submit that the Examiner has stipulated that Example 2 is enabled (see, Aug. 23, 2004 Office Action at page 4),

and Example 2 illustrates that MART-1 peptides are expressed on the cell surface after performing the methods of the invention. In particular, Example 2 shows that only when MART-1 peptides are displayed on cellular surfaces pursuant to the methods of the invention do cytotoxic T cells recognize and then kill those cells. Because cytotoxic T cells cannot recognize antigens within a cell, the MART-1 peptides must be displayed on the surface of the cells in order for those cells to be killed. Hence, the application clearly shows how to make cells that express antigens on their surfaces.

With regard to the Examiner's allegation that only certain cells are suitable for generating an immune response, Applicants submit that the specification describes and enables a variety of cell types that can display antigens and thereby generate an immune response. The types of immune responses contemplated by Applicants are disclosed at page 9 of Applicants' specification. The immune responses include stimulation of both humoral and cell-mediated immunity. Thus, the stimulation of cytotoxic cells is considered to be an immune response according to the specification. The generation of a cytotoxic T cell response to a foreign antigen presented on melanoma cells is described in Example 2 of Applicants' specification, and as indicated above, the Examiner has acknowledged that the method of Example 2 is enabled. Hence, *inter alia* cancer cells including melanoma cells are enabled.

Moreover, Applicants' specification discloses clearly that cells other than *classical* antigen-presenting cells are suitable for the method of the present invention. Applicants contemplate as antigen-presenting any cell capable of expressing or presenting on its surface a molecule that is administered or transported into its cytosol. Specification at page 8, lines 31-34. Cancer cells are specifically mentioned at page 9, lines 24 and 25 and in the examples. Costimulation of helper cells is not necessary to generate an immune response against cancer cells, as demonstrated in Applicants' Example 2.

With respect to photosensitizing agents, Applicants disclose several photosensitizing agents from a variety of unrelated classes. For example, $AlPcS_{2a}$ falls within the general class of phthalocyanines, $TPPS_4$ and $TPPS_{2a}$ are tetraphenylporphines, and chlorin e_6 is a chlorin. See page 12, lines 11-34.

Finally, as discussed in the personal interview, Applicants' Example 3 illustrates transport of HRP from the cytosol, and is not directed to showing surface presentation. Therefore, this example does not demonstrate a lack of antigen on the surface of the cells.

In view of the arguments above, Applicants submit that undue experimentation would not be required in order to practice the full scope of present invention. Applicants further note that a rejection for lack of enablement is improper when an enabled working example is present in the specification. Withdrawal of this rejection is respectfully requested.

2. New Matter

Claims 2-5 and 7-11 were rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner stated that no support exists for the language of claim 2, which the Examiner considers a broadening of the claimed invention. The Examiner stated: "the specification discloses only a method comprising the required cell surface expression by a class I MHC molecule on an antigen presenting cell." Office Action at page 6. This rejection is respectfully traversed.

As pointed out *supra*, Applicants' specification discloses clearly that cells other than *classical* antigen-presenting cells are suitable for the method of the present invention. In fact, Applicants contemplate as antigen-presenting any cell capable of expressing or presenting on its surface a molecule that is administered or transported into its cytosol. Specification at page 8, lines 31-34. Cancer cells are specifically mentioned at page 9, lines 24 and 25 and in the examples. Cancer cells are not classical antigen presenting cells. The Examiner's rejection appears to be based on a classical interpretation of the term *antigen-presenting*, rather than on the descriptive support present in Applicants' specification.

Moreover, Applicants submit that terminology relating to "viable" cells cannot be new matter because claim 2 has always specified that the cell be irradiated "without killing the cell." See claim 2 as filed. Further, it is clear from the specification and the claims that Applicants' cells must be viable. For example, the cells must be viable to perform the necessary cellular functions for displaying antigens on their surface after irradiation. Dead cells could not do so.

Hence, Applicants clearly were in possession of the claimed subject matter at the time of filing and withdrawal of this rejection is respectfully requested.

3. Written Description Requirement

Claim 7 was rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner objected specifically to the phrases *a lysomotropic weak base thereof* and *a derivative thereof* owing to the absence of disclosure of any species falling within the generic phrases. This rejection is respectfully traversed.

Applicants have cancelled the phrase *a derivative thereof* from claim 7, thereby rendering moot the aspect of the rejection germane thereto. Regarding the phrase *a lysomotropic weak base thereof,* Applicants submit that the phrase is a well-understood term of art that has been used widely in scientific publications for at least twenty-three years. See, for example, Helenius, A. et al., *J. Gen Virol.* **1982**, *58 Pt.1*, 47-61; Styrt, B., et al., *Blood* **1986**, *67*, 334-42; Zdolsek, J.M. et al., *Photochem. Photobiol.* **1990**, *51*, 67-76; and Antunes, F. et al., *Biochem. J.* **2001**, 356, 549-555. Copies of these documents are provided for the convenience of the Examiner.

As the above documents make clear, the phrase *a lysomotropic weak base* means a weak base that tends to have an effect on lysosomes. Numerous examples, such as acridine orange, ammonium chloride, chloroquine, methylamine, amantadine, etc. are known and described in the documents. The Federal Circuit in the recent decision, *Bilstad v. Wakalopulos*, Appeal 03-1528, decided October 7, 2004, required the PTO to consider the knowledge of the artisan and the predictability of the art when making a written description requirement rejection of a genus.

Applicants submit that the cited documents indicate that the skilled worker in the art would have a knowledge of the meaning of the phrase, such that further explanation and exemplification are unnecessary for the phrase to be described within the meaning of § 112. Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date December 21, 2004 By _____
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 21st day of December, 2004.

Patricia A. Hynes _____

Name Signature